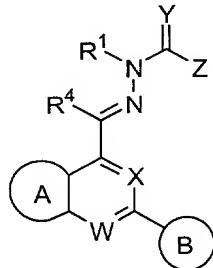


WHAT IS CLAIMED IS:

1. A compound having the formula:



2

3 wherein

4 W and X are independently selected from the group consisting of N and CH;

5 Y is selected from the group consisting of O, S and N(R);

6 wherein R is selected from the group consisting of H, CN, NO₂, (C₁-
7 C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-
8 C₁₀)alkenyl and (C₂-C₁₀)alkynyl;

9 Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl,
10 (C₄-C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³;

11 R¹, R² and R³ are independently selected from the group consisting of H, (C₁-
12 C₁₀)alkyl, (C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₁-C₁₀)heteroalkyl, (C₃-
13 C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl,
14 (C₃-C₁₀)cycloheteroalkyl, aryl, aryl(C₁-C₄)alkyl, aryl(C₁-C₄)heteroalkyl,
15 heteroaryl(C₁-C₄)alkyl, heteroaryl(C₁-C₄)heteroalkyl and perfluoro(C₁-
16 C₆)alkyl; and wherein when Z is NR²R³, R² and R³ can be combined to
17 form a 5- to 7-membered heterocyclyl ring;

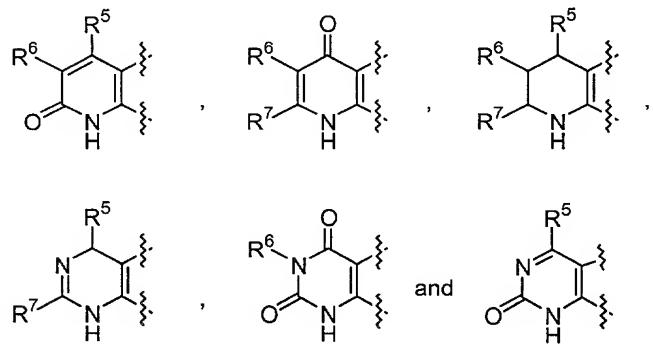
18 R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl,
19 (C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;

20 A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,
21 said ring system being mono- or bicyclic wherein said mono- or bicyclic
22 rings are selected from the group consisting of five- and six-membered
23 rings that are aromatic or partially or completely saturated; and

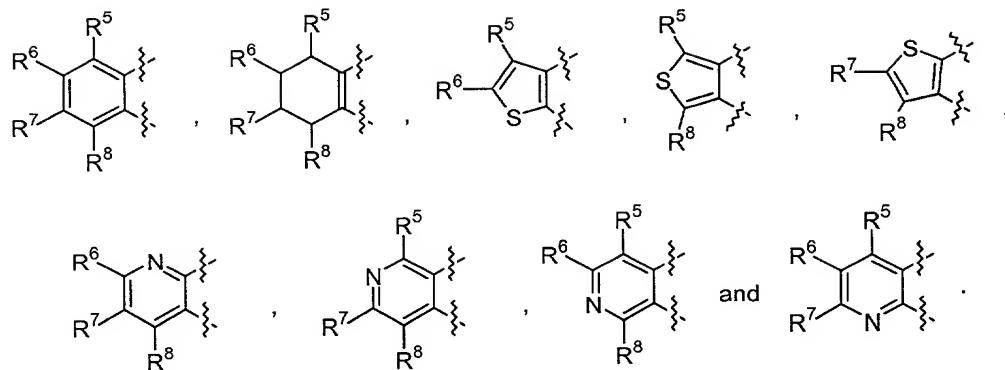
24 B is a substituted or unsubstituted five- or six-membered ring which is aromatic or
25 partially or completely saturated, containing at least one nitrogen atom,
26 and from 0 to 3 additional heteroatoms, wherein the B ring substituents are
27 selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl,

28 perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl,
29 (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-
30 C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-
31 C₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C₁-C₆)acyl, (C₁-
32 C₆)acylamino, (C₁-C₆)alkoxycarbonyl, (C₁-C₆)alkoxycarbonyl(C₁-
33 C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy.

- 1 2. A compound of claim 1, wherein W is N and X is CH.
1 3. A compound of claim 1, wherein W is N and X is N.
1 4. A compound of claim 1, wherein W is CH and X is N.
1 5. A compound of claim 1, wherein W is CH and X is CH.
1 6. A compound of claim 2, wherein Y is selected from the group
2 consisting of O and S.
1 7. A compound of claim 2, wherein Y is O.
1 8. A compound of claim 2, wherein Y is S.
1 9. A compound of claim 2, wherein Z is NR²R³.
1 10. A compound of claim 6, wherein R⁴ is H.
1 11. A compound of claim 1, wherein A is selected from the group
2 consisting of:



- 1 12. A compound of claim 1, wherein A is selected from the group
2 consisting of:



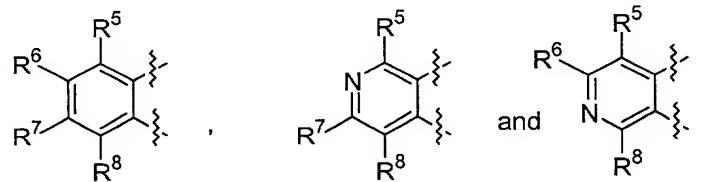
3

4 wherein

5 R^5 , R^6 , R^7 and R^8 are independently selected from the group consisting of H,
 6 halogen, CF_3 , $(C_1\text{-}C_6)$ alkyl, $(C_2\text{-}C_6)$ alkenyl, $(C_2\text{-}C_6)$ alkynyl, $(C_1\text{-}$
 7 $C_6)$ heteroalkyl, $(C_1\text{-}C_6)$ alkoxy, $(C_1\text{-}C_6)$ thioalkoxy, amino, $(C_1\text{-}$
 8 $C_6)$ alkylamino, di $(C_1\text{-}C_6)$ alkylamino, $(C_3\text{-}C_{10})$ cycloalkyl, $(C_4\text{-}$
 9 $C_{10})$ cycloalkyl-alkyl, $(C_3\text{-}C_{10})$ cycloheteroalkyl, $(C_3\text{-}C_{10})$ cycloheteroalkyl-
 10 alkyl, cyano, nitro, $(C_1\text{-}C_6)$ acyl, $(C_1\text{-}C_6)$ acylamino, $(C_1\text{-}C_6)$ alkoxycarbonyl,
 11 $(C_1\text{-}C_6)$ alkoxycarbonyl $(C_1\text{-}C_6)$ alkyl, $CONH_2$, $CO\text{-}NH\text{-}(C_1\text{-}C_6)$ alkyl, $CO\text{-}$
 12 $N[(C_1\text{-}C_6)$ alkyl] $_2$, SO_2NH_2 , $SO_2NH\text{-}(C_1\text{-}C_6)$ alkyl, $SO_2N\text{-}[(C_1\text{-}C_6)$ alkyl] $_2$
 13 and $(C_1\text{-}C_6)$ heteroalkoxy; or two adjacent R groups selected from R^5 , R^6 ,
 14 R^7 and R^8 , can be linked together to form a new 5- or 6-membered
 15 carbocyclic or heterocyclic ring.

1 13. A compound of claim 12, wherein W is N; X is CH; Y is O or S;

2 and A is selected from the group consisting of:



3

1 14. A compound of claim 1, wherein B contains a nitrogen atom at a
 2 position two atoms away from the atom attaching B to the remainder of the molecule.

1 15. A compound of claim 1, wherein B contains a nitrogen atom at the
 2 point of attachment of B to the remainder of the molecule.

1 16. A compound of claim 1, wherein B is selected from the group
 2 consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-

3 1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-
4 triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

1 17. A compound of claim 1, wherein B is selected from the group
2 consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted
3 thiazolyl and substituted or unsubstituted triazolyl.

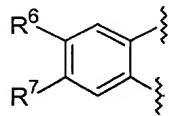
1 18. A compound of claim 13, wherein B contains a nitrogen atom at a
2 position two atoms away from the atom attaching B to the remainder of the molecule.

1 19. A compound of claim 13, wherein B contains a nitrogen atom at
2 the point of attachment of B to the remainder of the molecule.

1 20. A compound of claim 13, wherein B is selected from the group
2 consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-
3 1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-
4 triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

1 21. A compound of claim 13, wherein B is selected from the group
2 consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted
3 thiazolyl and substituted or unsubstituted triazolyl.

1 22. A compound of claim 1, wherein W is N; X is CH; Y is O or S; Z
2 is H, CH₃, NH₂ or NHCH₃; R¹ is H, (C₁-C₆)alkyl, (C₁-C₁₀)heteroalkyl, (C₄-
3 C₁₀)cycloheteroalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, aryl(C₁-C₄)alkyl, aryl(C₁-
4 C₄)heteroalkyl, heteroaryl(C₁-C₄)alkyl, heteroaryl(C₁-C₄)heteroalkyl, or perfluoro(C₁-
5 C₆)alkyl; R⁴ is H; A represents



7 wherein R⁶ and R⁷ are independently selected from the group consisting of
8 H, halogen, CF₃, CF₃O, (C₁-C₄)alkyl, (C₂-C₄)alkenyl, (C₂-C₄)alkynyl, (C₁-C₄)heteroalkyl,
9 (C₃-C₁₀)cycloheteroalkyl-alkyl and cyano; and B is a five-membered aromatic ring
10 system containing at least one nitrogen atom.

1 23. A compound of claim 22, wherein Y is S.

1 **24.** A compound of claim **22**, wherein Z is NR²R³.

1 **25.** A compound of claim **22**, wherein Z is NH₂.

1 **26.** A compound of claim **22**, wherein R¹ is (C₁-C₆)alkyl, (C₁-
2 C₆)heteroalkyl or (C₃-C₁₀)cycloheteroalkyl-alkyl.

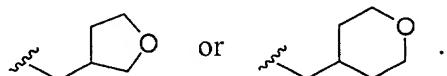
1 **27.** A compound of claim **22**, wherein B is a five-membered aromatic
2 ring system containing 1-2 nitrogen atoms and 0-1 sulfur atoms.

1 **28.** A compound of claim **27**, wherein B is unsubstituted or substituted
2 by (C₁-C₃)alkyl, CF₃, cyano, or halogen.

1 **29.** A compound of claim **22**, wherein Z is NH₂; R⁶ is selected from the
2 group consisting of H, halogen, CF₃, CF₃O, (C₁-C₄)alkyl, (C₂-C₄)alkenyl, (C₁-
3 C₄)heteroalkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl and cyano, wherein the alkyl, alkenyl and
4 heteroalkyl groups optionally bear additional substituents selected from cyano,
5 carboxamido, (C₁-C₃)alkylsulfonyl or (C₁-C₃)alkoxy; and R⁷ is selected from the group
6 consisting of H, halogen, CF₃, CF₃O, (C₁-C₄)alkyl, (C₂-C₄)alkenyl, (C₂-C₄)alkynyl, (C₁-
7 C₄)heteroalkyl and cyano.

1 **30.** A compound of claim **29**, wherein R⁶ is selected from the group
2 consisting of CH₂(CH₂)_mCN, CH₂(CH₂)_nSO₂CH₃ and CH₂(CH₂)_nOCH₃, wherein the
3 subscript n is an integer from 0 to 2.

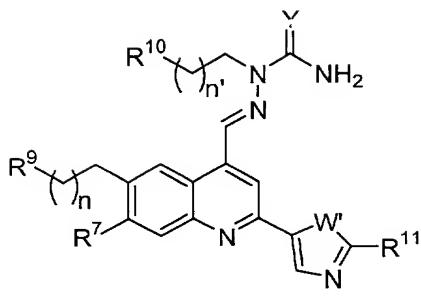
1 **31.** A compound of claim **29**, wherein R⁶ is



1 **32.** A compound of claim **29**, wherein R⁷ is selected from H, halogen,
2 CF₃ and (C₁-C₄)alkyl.

1 **33.** A compound of claim **29**, wherein R⁷ is methyl.

1 **34.** A compound of claim **1**, having the formula:



2

3 wherein Y is O, S or N-CN; W' is N(CH₃), N(CF₃), N(CH₂CH₃), O or S; the subscripts n
4 and n' are independently integers from 0 to 3; R⁷ is H, halogen, CF₃, CF₃O, (C₁-C₄)alkyl,
5 (C₂-C₄)alkenyl, (C₂-C₄)alkynyl, (C₁-C₄)heteroalkyl or cyano; R⁹ is CN, CONH₂, CO-NH-
6 (C₁-C₆)alkyl, CO-N[(C₁-C₆)alkyl]₂, CO-NH-(C₁-C₆)heteroalkyl, CO-N[(C₁-
7 C₆)heteroalkyl]₂, S(O)_{n''}-(C₁-C₆)alkyl, S(O)_{n''}-(C₁-C₆)heteroalkyl, heteroaryl, (C₁-
8 C₆)alkoxy or (C₃-C₆)cycloheteroalkyl, wherein each n'' is independently an integer of 0 to
9 2; R¹⁰ is NH₂, NH-(C₁-C₆)alkyl, N[(C₁-C₆)alkyl]₂, NH-(C₁-C₆)heteroalkyl, N[(C₁-
10 C₆)heteroalkyl]₂, (C₁-C₆)heteroalkyl, S(O)_{n''}-(C₁-C₆)alkyl, S(O)_{n''}-(C₁-C₆)heteroalkyl, aryl,
11 heteroaryl, O-(C₁-C₆)alkyl, O-(C₁-C₆)heteroalkyl or (C₃-C₈)cycloheteroalkyl; and R¹¹ is
12 H, CF₃, NH₂, NH-(C₁-C₆)alkyl, N[(C₁-C₆)alkyl]₂, halogen or (C₁-C₃)alkyl.

1 **35.** A compound of claim 34, wherein Y is O or S; W' is N-CH₃; n is
2 2; n' is 1-3; R⁹ is cyano, CONH₂, SO₂-(C₁-C₆)alkyl, (C₁-C₆)alkoxy or (C₃-
3 C₆)cycloheteroalkyl; R¹⁰ is NH-(C₁-C₆)alkyl, N[(C₁-C₆)alkyl]₂, NH-(C₁-C₆)heteroalkyl,
4 N[(C₁-C₆)heteroalkyl]₂, O-(C₁-C₆)alkyl, O-(C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy or (C₃-
5 C₈)cycloheteroalkyl; and R¹¹ is H.

1 **36.** A compound of claim 22, wherein B contains a nitrogen atom at a
2 position two atoms away from the atom attaching B to the remainder of the molecule.

1 **37.** A compound of claim 22, wherein B contains a nitrogen atom at
2 the point of attachment of B to the remainder of the molecule.

1 **38.** A compound of claim 22, wherein B is selected from the group
2 consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted
3 thiazolyl and substituted or unsubstituted triazolyl.

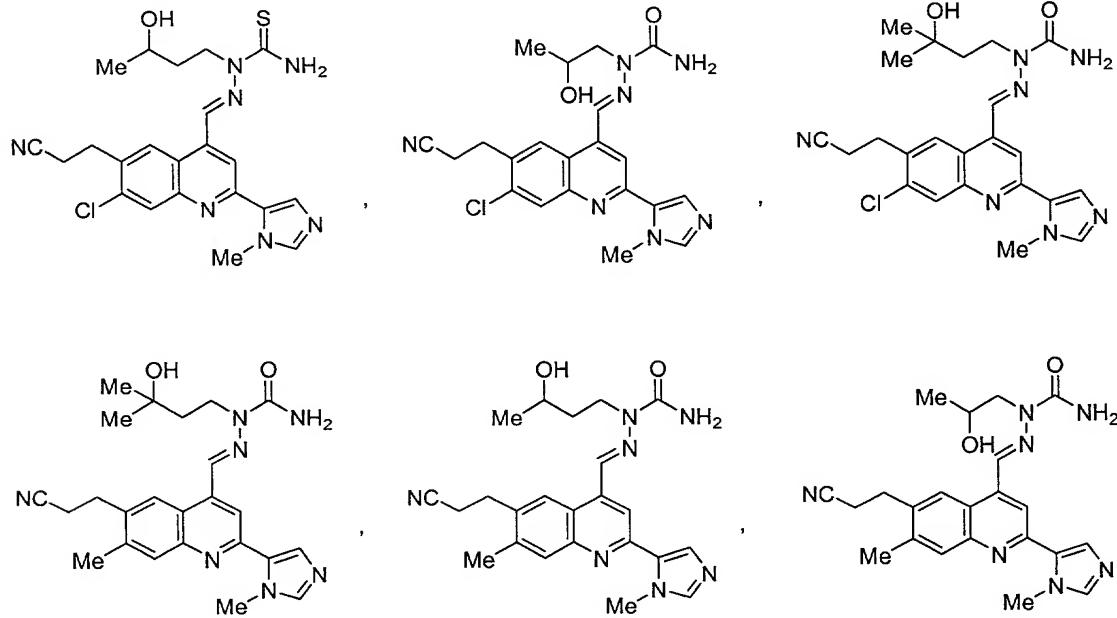
1 **39.** A compound of claim 22, wherein B is selected from the group
2 consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-

3 1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-
4 triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

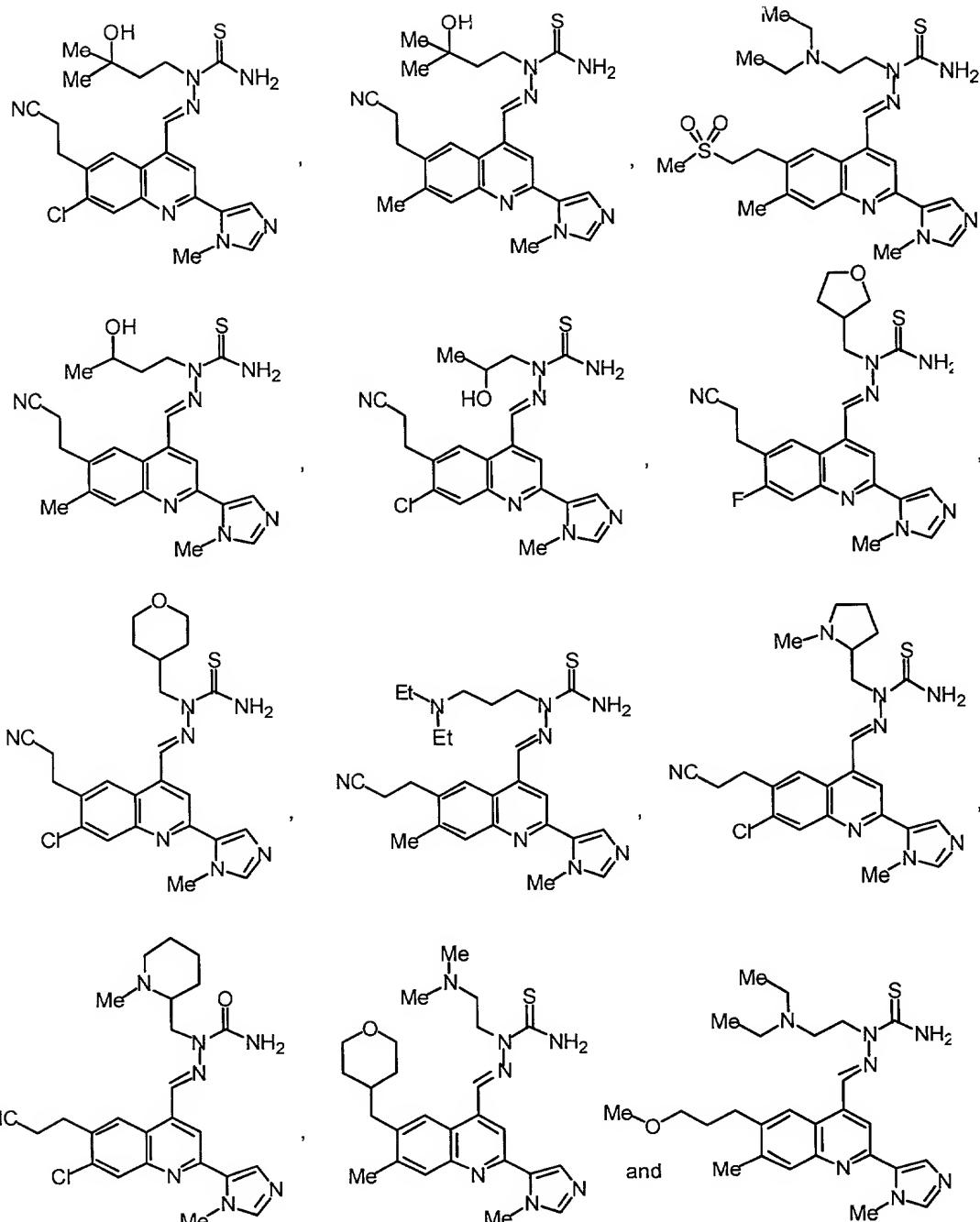
1 40. A compound of claim 1, wherein Y is S; Z is NH₂ and R¹ is (C₁-
2 C₆)alkyl.

1 41. A compound of claim 40, wherein R¹ is methyl.

1 42. A compound of claim 1, wherein said compound is selected from the
2 group consisting of:

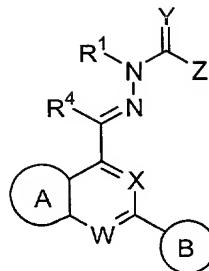


3



4
5

1 43. A composition comprising a pharmaceutically acceptable excipient
2 and a compound having the formula:



3

4 wherein

5 W and X are independently selected from the group consisting of N and CH;

6 Y is selected from the group consisting of O, S and N(R);

7 wherein R is selected from the group consisting of H, CN, NO₂, (C₁-
8 C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-
9 C₁₀)alkenyl and (C₂-C₁₀)alkynyl;

10 Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl,

11 (C₄-C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³;

12 R¹, R² and R³ are independently selected from the group consisting of H, (C₁-
13 C₁₀)alkyl, (C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₂-C₁₀)heteroalkyl, (C₃-
14 C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl,
15 (C₃-C₁₀)cycloheteroalkyl, aryl, aryl(C₁-C₄)alkyl, aryl(C₂-C₄)heteroalkyl,
16 heteroaryl(C₂-C₄)alkyl, heteroaryl(C₂-C₄)heteroalkyl and perfluoro(C₁-
17 C₆)alkyl; and wherein when Z is NR²R³, R² and R³ can be combined to
18 form a 5- to 7-membered ring; and wherein when Y is N(R), R and R¹ are
19 optionally combined to form a 5- to 7-membered ring;

20 R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl,
21 (C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;

22 A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,
23 said ring system being mono- or bicyclic wherein said mono- or bicyclic
24 rings are selected from the group consisting of five- and six-membered
25 rings that are aromatic or partially or completely saturated; and

26 B is a substituted or unsubstituted five- or six-membered ring which is aromatic or
27 partially or completely saturated, containing at least one nitrogen atom,
28 and from 0 to 3 additional heteroatoms, wherein the B ring substituents are
29 selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl,
30 perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl,
31 (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-

C_6)alkylamino, (C_3 - C_{10})cycloalkyl, (C_4 - C_{10})cycloalkyl-alkyl, (C_3 - C_{10})cycloheteroalkyl, cyano, nitro, sulfonamido, (C_1 - C_6)acyl, (C_1 - C_6)acylamino, (C_2 - C_6)alkoxycarbonyl, (C_2 - C_6)alkoxycarbonyl(C_1 - C_6)alkyl, carboxamido and (C_1 - C_6)heteroalkoxy.

44. A composition in accordance with claim 43, wherein W is N and X

45. A composition in accordance with claim 43, wherein W is N and X

46. A composition in accordance with claim 43, wherein W is CH and

47. A composition in accordance with claim 43, wherein W is CH and

48. A composition in accordance with claim 43, wherein Y is selected from the group consisting of O and S.

49. A composition in accordance claim 43, wherein Y is O.

50. A composition in accordance claim 43, wherein Y is S.

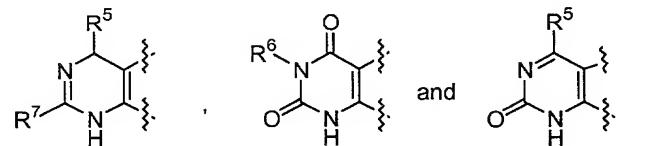
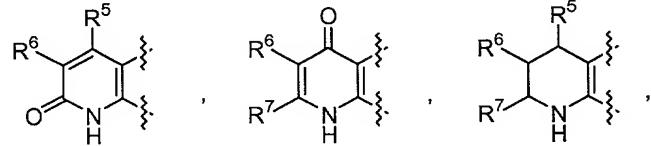
51. A composition in accordance claim 43, wherein Z is NR^2R^3 .

52. A composition in accordance with claim 48, wherein R⁴ is H.

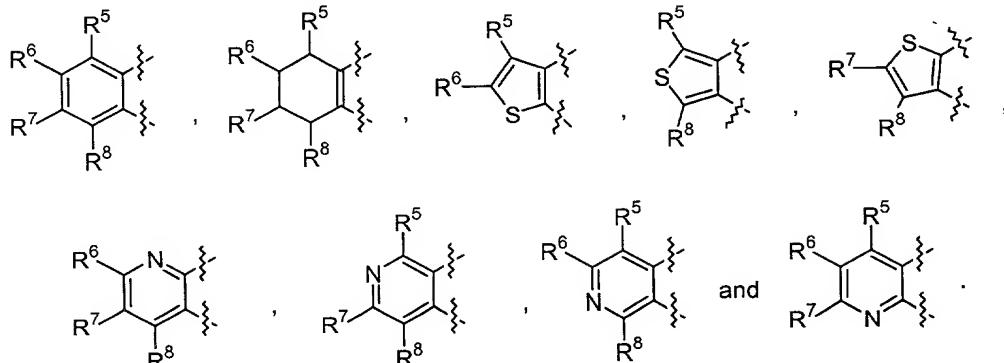
53. A composition in accordance with claim 43, wherein A is sele

up consisting of:

up consisting of:



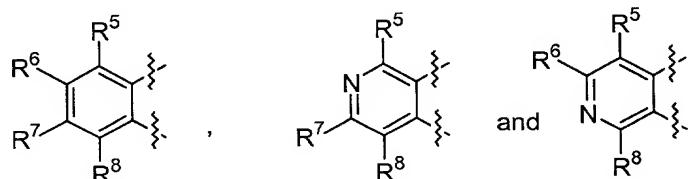
1 **54.** A composition in accordance with claim 43, wherein A is selected
2 from the group consisting of:



3 wherein

4 R⁵, R⁶, R⁷ and R⁸ are independently selected from the group consisting of H,
5 halogen, CF₃, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-
6 C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-
7 C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-
8 C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, (C₃-C₁₀)cycloheteroalkyl-
9 alkyl, cyano, nitro, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₂-C₆)alkoxycarbonyl,
10 (C₃-C₆)alkoxycarbonylalkyl, CONH₂, CO-NH-(C₁-C₆)alkyl, CO-N[(C₁-
11 C₆)alkyl]₂, SO₂NH₂, SO₂NH-(C₁-C₆)alkyl, SO₂N-[(C₁-C₆)alkyl]₂ and (C₁-
12 C₆)heteroalkoxy; or two adjacent R groups can be linked together to form
13 a new 5- or 6-membered carbocyclic or heterocyclic ring.
14

1 **55.** A composition in accordance with claim 43, wherein W is N; X is
2 CH; Y is O or S; and A is selected from the group consisting of:



1 **56.** A composition in accordance with claim 43, wherein B contains a
2 nitrogen atom at a position two atoms away from the atom attaching B to the remainder of
3 the molecule.

1 **57.** A composition in accordance with claim 43, wherein B contains a
2 nitrogen atom at the point of attachment of B to the remainder of the molecule.

1 **58.** A composition in accordance with claim 43, wherein B is selected
2 from the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-
3 methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-
4 methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

1 **59.** A composition in accordance with claim 43, wherein B is selected
2 from the group consisting of substituted or unsubstituted imidazolyl, substituted or
3 unsubstituted thiazolyl and substituted or unsubstituted triazolyl.

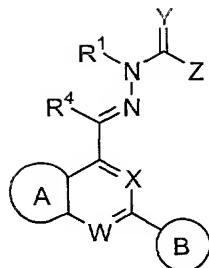
1 **60.** A composition in accordance with claim 55, wherein B contains a
2 nitrogen atom at a position two atoms away from the atom attaching B to the remainder of
3 the molecule.

1 **61.** A composition in accordance with claim 55, wherein B contains a
2 nitrogen atom at the point of attachment of B to the remainder of the molecule.

1 **62.** A composition in accordance with claim 55, wherein B is selected
2 from the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-
3 methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-
4 methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

1 **63.** A composition in accordance with claim 55, wherein B is selected
2 from the group consisting of substituted or unsubstituted imidazolyl, substituted or
3 unsubstituted thiazolyl and substituted or unsubstituted triazolyl.

1 **64.** A method for treating an inflammatory, metabolic or malignant
2 condition, said method comprising administering to a subject in need of such treatment,
3 an effective amount of a compound having the formula:



4

5 wherein

6 W and X are independently selected from the group consisting of N and CH;

7 Y is selected from the group consisting of O, S and N(R);

8 wherein R is selected from the group consisting of H, CN, NO₂, (C₁-9 C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-10 C₁₀)alkenyl and (C₂-C₁₀)alkynyl;11 Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl,12 (C₄-C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³;13 R¹, R² and R³ are independently selected from the group consisting of H, (C₁-14 C₁₀)alkyl, (C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₂-C₁₀)heteroalkyl, (C₃-15 C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl,16 (C₃-C₁₀)cycloheteroalkyl, aryl, aryl(C₁-C₄)alkyl, aryl(C₂-C₄)heteroalkyl,17 heteroaryl(C₂-C₄)alkyl, heteroaryl(C₂-C₄)heteroalkyl and perfluoro(C₁-18 C₆)alkyl; and wherein when Z is NR²R³, R² and R³ can be combined to19 form a 5- to 7-membered ring; and wherein when Y is N(R), R and R¹ are

20 optionally combined to form a 5- to 7-membered ring;

21 R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl,22 (C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;

23 A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,

24 said ring system being mono- or bicyclic wherein said mono- or bicyclic

25 rings are selected from the group consisting of five- and six-membered

26 rings that are aromatic or partially or completely saturated; and

27 B is a substituted or unsubstituted five- or six-membered ring which is aromatic or

28 partially or completely saturated, containing at least one nitrogen atom,

29 and from 0 to 3 additional heteroatoms, wherein the B ring substituents are

30 selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl,31 perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl,32 (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-

1 **65.** A method in accordance with claim **64**, wherein W is N and X is
2 CH₃.

66. A method in accordance with claim 64, wherein W is N and X is N.

1 67. A method in accordance with claim 64, wherein W is CH and X is
2 N.

1 **68.** A method in accordance with claim **64**, wherein W is CH and X is
2 CH.

1 **69.** A method in accordance with claim **65**, wherein Y is selected from
2 the group consisting of O and S.

1 70. A method in accordance with claim 65, wherein Y is O.

1 71. A method in accordance with claim 65, wherein Y is S.

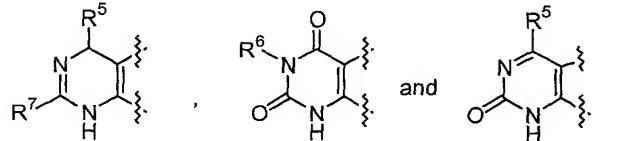
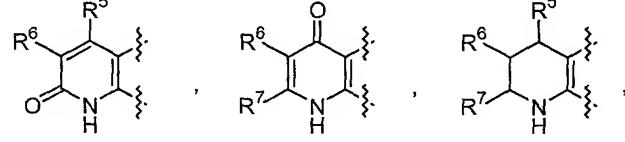
1 72. A method in accordance with claim 65, wherein Z is NR^2R^3 .

1 73. A method in accordance with claim 69, wherein R⁴ is H.

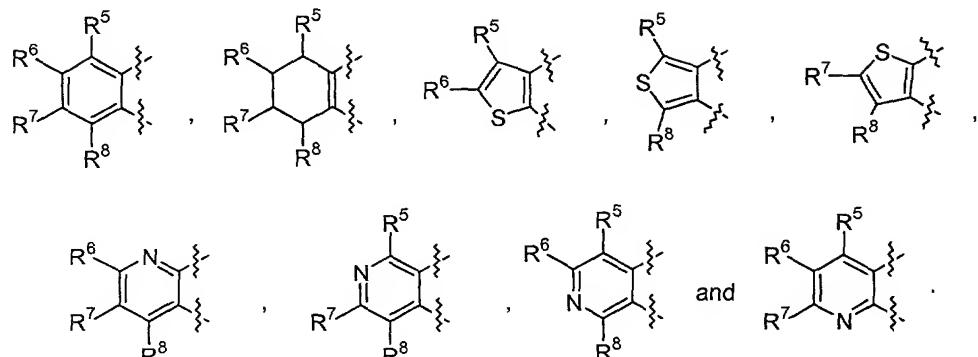
74. A method in accordance with claim 64, wherein A is selected

2 the group consisting of:

2 the group consisting of:



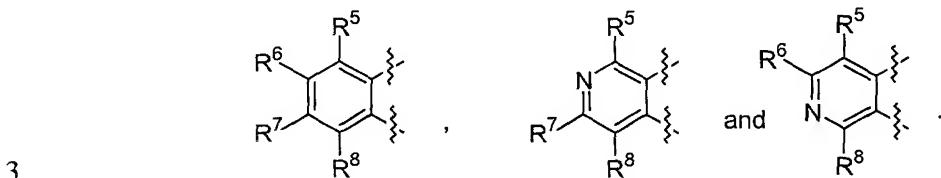
1 75. A method in accordance with claim 64, wherein A is selected from
2 the group consisting of:



3 wherein

4 R⁵, R⁶, R⁷ and R⁸ are independently selected from the group consisting of H,
5 halogen, CF₃, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-
6 C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-
7 C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-
8 C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, (C₃-C₁₀)cycloheteroalkyl-
9 alkyl, cyano, nitro, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₂-C₆)alkoxycarbonyl,
10 (C₃-C₆)alkoxycarbonylalkyl, CONH₂, CO-NH-(C₁-C₆)alkyl, CO-N[(C₁-
11 C₆)alkyl]₂, SO₂NH₂, SO₂NH-(C₁-C₆)alkyl, SO₂N-[(C₁-C₆)alkyl]₂ and (C₁-
12 C₆)heteroalkoxy; or two adjacent R groups can be linked together to form
13 a new 5- or 6-membered carbocyclic or heterocyclic ring.

1 76. A method in accordance with claim 64, wherein W is N; X is CH;
2 Y is O or S; and A is selected from the group consisting of:



1 77. A method in accordance with claim 64, wherein B contains a
2 nitrogen atom at a position two atoms away from the atom attaching B to the remainder of
3 the molecule.

1 **78.** A method in accordance with claim 64, wherein B contains a
2 nitrogen atom at the point of attachment of B to the remainder of the molecule.

1 **79.** A method in accordance with claim 64, wherein B is selected from
2 the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-
3 methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-
4 methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

1 **80.** A method in accordance with claim 64, wherein B is selected from
2 the group consisting of substituted or unsubstituted imidazolyl, substituted or
3 unsubstituted thiazolyl and substituted or unsubstituted triazolyl.

1 **81.** A method in accordance with claim 76, wherein B contains a
2 nitrogen atom at a position two atoms away from the atom attaching B to the remainder of
3 the molecule.

1 **82.** A method in accordance with claim 76, wherein B contains a
2 nitrogen atom at the point of attachment of B to the remainder of the molecule.

1 **83.** A method in accordance with claim 76, wherein B is selected from
2 the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-
3 methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-
4 methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

1 **84.** A method in accordance with claim 76, wherein B is selected from
2 the group consisting of substituted or unsubstituted imidazolyl, substituted or
3 unsubstituted thiazolyl and substituted or unsubstituted triazolyl.

1 **85.** A method in accordance with claim 64, wherein said compound is
2 administered orally.

1 **86.** A method in accordance with claim 64, wherein said compound is
2 administered topically.

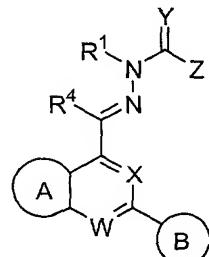
1 **87.** A method in accordance with claim 64, wherein said compound is
2 administered intravenously or intramuscularly.

1 **88.** A method in accordance with claim 64, wherein said compound is
2 administered in combination with a second therapeutic agent, said second therapeutic
3 agent being a member selected from the group consisting of prednisone, dexamethasone,
4 beclomethasone, methylprednisone, betamethasone, hydrocortisone, methotrexate,
5 cyclosporin, rapamycin, tacrolimus, antihistamine drugs, TNF antibodies, IL-1 antibodies,
6 soluble TNF receptors, soluble IL-1 receptors, TNF or IL-1 receptor antagonists, non-
7 steroidal antiinflammatory agents, COX-2 inhibitors, antidiabetic agents, and anticancer
8 agents.

1 **89.** A method in accordance with claim 88, wherein said administering
2 is sequential.

1 **90.** A method in accordance with claim 64, wherein said inflammatory,
2 metabolic or malignant condition is selected from the group consisting of rheumatoid
3 arthritis, inflammatory bowel disease, psoriasis, cancer, diabetes and septic shock.

1 **91.** A method for treating a condition or disorder mediated by IKK,
2 comprising
3 administering to a subject in need thereof a therapeutically effective
4 amount of a compound having the formula:



5
6 wherein

7 W and X are independently selected from the group consisting of N and CH;
8 Y is selected from the group consisting of O, S and N(R);

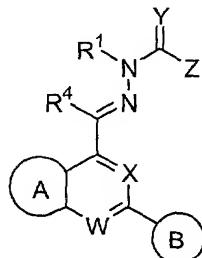
9 wherein R is selected from the group consisting of H, CN, NO₂, (C₁-
10 C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-
11 C₁₀)alkenyl and (C₂-C₁₀)alkynyl;

12 Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl,
13 (C₄-C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³;

WO 2009/035330 A1

14 R¹, R² and R³ are independently selected from the group consisting of H, (C₁-
15 C₁₀)alkyl, (C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₁-C₁₀)heteroalkyl, (C₃-
16 C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl,
17 (C₃-C₁₀)cycloheteroalkyl, aryl, aryl(C₁-C₄)alkyl, aryl(C₁-C₄)heteroalkyl,
18 heteroaryl(C₁-C₄)alkyl, heteroaryl(C₁-C₄)heteroalkyl and perfluoro(C₁-
19 C₆)alkyl; and wherein when Z is NR²R³, R² and R³ can be combined to
20 form a 5- to 7-membered heterocycl ring;
21 R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl,
22 (C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;
23 A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,
24 said ring system being mono- or bicyclic wherein said mono- or bicyclic
25 rings are selected from the group consisting of five- and six-membered
26 rings that are aromatic or partially or completely saturated; and
27 B is a substituted or unsubstituted five- or six-membered ring which is aromatic or
28 partially or completely saturated, containing at least one nitrogen atom,
29 and from 0 to 3 additional heteroatoms, wherein the B ring substituents are
30 selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl,
31 perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl,
32 (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-
33 C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-
34 C₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C₁-C₆)acyl, (C₁-
35 C₆)acylamino, (C₁-C₆)alkoxycarbonyl, (C₁-C₆)alkoxycarbonyl(C₁-
36 C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy.

1 92. A method for modulating IKK, comprising
2 contacting a cell with a compound having the formula:



3 wherein

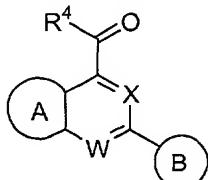
4 5 W and X are independently selected from the group consisting of N and CH;

6 Y is selected from the group consisting of O, S and N(R);
7 wherein R is selected from the group consisting of H, CN, NO₂, (C₁-
8 C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-
9 C₁₀)alkenyl and (C₂-C₁₀)alkynyl;
10 Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl,
11 (C₄-C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³;
12 R¹, R² and R³ are independently selected from the group consisting of H, (C₁-
13 C₁₀)alkyl, (C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₁-C₁₀)heteroalkyl, (C₃-
14 C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl,
15 (C₃-C₁₀)cycloheteroalkyl, aryl, aryl(C₁-C₄)alkyl, aryl(C₁-C₄)heteroalkyl,
16 heteroaryl(C₁-C₄)alkyl, heteroaryl(C₁-C₄)heteroalkyl and perfluoro(C₁-
17 C₆)alkyl; and wherein when Z is NR²R³, R² and R³ can be combined to
18 form a 5- to 7-membered heterocyclic ring;
19 R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl,
20 (C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;
21 A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,
22 said ring system being mono- or bicyclic wherein said mono- or bicyclic
23 rings are selected from the group consisting of five- and six-membered
24 rings that are aromatic or partially or completely saturated; and
25 B is a substituted or unsubstituted five- or six-membered ring which is aromatic or
26 partially or completely saturated, containing at least one nitrogen atom,
27 and from 0 to 3 additional heteroatoms, wherein the B ring substituents are
28 selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl,
29 perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl,
30 (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-
31 C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-
32 C₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C₁-C₆)acyl, (C₁-
33 C₆)acylamino, (C₁-C₆)alkoxycarbonyl, (C₁-C₆)alkoxycarbonyl(C₁-
34 C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy.

1 93. The method of Claim 92, wherein said compound is an IKK
2 inhibitor.

94. The method of Claim 92, wherein said compound is an IKK

1 **95.** A method for the preparation of antiinflammation agents
2 comprising contacting a precursor compound having the formula:



3
4 wherein

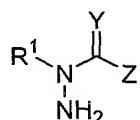
W and X are independently selected from the group consisting of N and CH;

R^4 is selected from the group consisting of H, (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl, (C_4-C_7) cycloalkyl-alkyl, (C_2-C_6) alkenyl and (C_2-C_6) alkynyl;

A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system, said ring system being mono- or bicyclic wherein said mono- or bicyclic rings are selected from the group consisting of five- and six-membered rings that are aromatic or partially or completely saturated; and

B is a substituted or unsubstituted five- or six-membered ring which is aromatic or partially or completely saturated, containing at least one nitrogen atom, and from 0 to 3 additional heteroatoms, wherein the B ring substituents are selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl, perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₂-C₆)alkoxycarbonyl, (C₂-C₆)alkoxycarbonyl(C₁-C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy

22 with a compound having the formula:



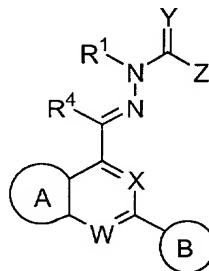
24 wherein

25 Y is selected from the group consisting of O, S and N(R);

26 wherein R is selected from the group consisting of H, CN, NO₂, (C₁-
27 C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-
28 C₁₀)alkenyl and (C₂-C₁₀)alkynyl;

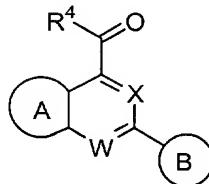
29 Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl,
30 (C₄-C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³;
31 R¹, R² and R³ are independently selected from the group consisting of H, (C₁-
32 C₁₀)alkyl, (C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₂-C₁₀)heteroalkyl, (C₃-
33 C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl,
34 (C₃-C₁₀)cycloheteroalkyl, aryl, aryl(C₁-C₄)alkyl, aryl(C₂-C₄)heteroalkyl,
35 heteroaryl(C₂-C₄)alkyl, heteroaryl(C₂-C₄)heteroalkyl and perfluoro(C₁-
36 C₆)alkyl; and wherein when Z is NR²R³, R² and R³ can be combined to
37 form a 5- to 7-membered ring; and wherein when Y is N(R), R and R¹ are
38 optionally combined to form a 5- to 7-membered ring;

39 under conditions sufficient to produce compounds having the formula:



41 wherein each of A, B, R¹, R⁴, W, X, Y and Z have the meanings provided above.

1 **96.** A compound having the formula:



2 wherein

4 W and X are independently selected from the group consisting of N and CH;
5 R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl,
6 (C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;
7 A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,
8 said ring system being mono- or bicyclic wherein said mono- or bicyclic

9 rings are selected from the group consisting of five- and six-membered
10 rings that are aromatic or partially or completely saturated; and

11 B is a substituted or unsubstituted five- or six-membered ring which is aromatic or
12 partially or completely saturated, containing at least one nitrogen atom,
13 and from 0 to 3 additional heteroatoms, wherein the B ring substituents are
14 selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl,
15 perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl,
16 (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-
17 C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-
18 C₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C₁-C₆)acyl, (C₁-
19 C₆)acylamino, (C₂-C₆)alkoxycarbonyl, (C₂-C₆)alkoxycarbonyl(C₁-
20 C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy.

1 97. A compound of claim 96, wherein R⁴ is hydrogen.

1 98. A compound of claim 96, wherein R⁴ is hydrogen, Y is O or S, and
2 Z is NR²R³.

1 99. A compound of claim 96, wherein R⁴ is hydrogen, Y is O or S, Z is
2 NR²R³, and B contains a nitrogen atom at a position two atoms away from the atom
3 attaching B to the remainder of the molecule.

1 100. A compound of claim 96, B contains a nitrogen atom at the point of
2 attachment of B to the remainder of the molecule.

1 101. A compound of claim 99, wherein B is selected from the group
2 consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-
3 1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-
4 triazolyl, and 4-methyl-1,2,4-triazol-3-yl.